



9491-013-27.ST25

SEQUENCE LISTING

RECEIVED

SEP 16 2003

TECH CENTER 1600/2900

<110> Adams, Camellia W.
Carter, Paul J.
Fendly, Brian M.
Gurney, Austin L.

<120> Agonist Antibodies

<130> 9491-013-27

<140> US 09/138,091

<141> 1998-08-21

<150> US 60/056,736

<151> 1997-08-22

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Pro Ser Phe Glu Asp Gln Val Thr Met Ser
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 Val Ser
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 Asp Tyr Tyr Met Ser
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 Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala
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gac tct gtg aag ggc cga ttc acc atc tcc
 Asp Ser Val Lys Gly Arg Phe Thr Ile Ser

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Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
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Lys Gly Arg Phe Thr Ile Ser
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Trp Ser Gly Glu Asp Ala Phe Asp Ile
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Arg Ala Ser Glu Gly Ile Tyr His Trp Leu Ala
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Lys Ala Ser Ser Leu Ala Ser
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 Asp Arg Gly Ser Tyr Gly Met Asp Val
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 Gly Ile Ser Phe Asp Gly Arg Ser Glu Tyr Tyr Ala
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36

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 Asp Ser Val Gln Gly Arg Phe Thr Ile Ser
 15 20 22

66

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Gln Gly Arg Phe Thr Ile Ser

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 Gly Ala His Tyr Gly Phe Asp Ile
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24

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<400> 34
 Gly Ala His Tyr Gly Phe Asp Ile
 1 5

<210> 35
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 <212> DNA
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33

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 <212> DNA
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 Ser His Asn Met Asn
 1 5

15

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gac tca gtg aag ggc cga ttc acc atc tcc
 Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
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 Lys Gly Arg Phe Thr Ile Ser
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 Asp Arg Gly Ser Thr Gly Met Asp Val
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<210> 42
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 Ser Tyr Tyr Trp Ser
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 <211> 63
 <212> DNA
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 Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro
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tcc ctc aag agt cga gtc acc ata tca 63
 Ser Leu Lys Ser Arg Val Thr Ile Ser
 15 20

<210> 45
 <211> 21
 <212> PRT
 <213> Homo sapiens

<400> 45
 Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
 1 5 10 15

Ser Arg Val Thr Ile Ser
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<210> 46
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<400> 46 18
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 Gly Arg Tyr Phe Asp Val
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<210> 47
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 <212> PRT
 <213> Homo sapiens

<400> 47
 Gly Arg Tyr Phe Asp Val
 1 5

<210> 48
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 <212> DNA
 <213> Homo sapiens

<400> 48 36
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 Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
 1 5 10

gtc tcc 42
 Val Ser
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<210> 49
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<400> 49.
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<210> 50
 <211> 21
 <212> DNA
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<400> 50
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 Glu Gly Ser Lys Arg Pro Ser
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 <212> PRT
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<400> 51
 Glu Gly Ser Lys Arg Pro Ser
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<210> 52
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<400> 52
 agc tca tat aca acc agg agc act cga gtt
 Ser Ser Tyr Thr Thr Arg Ser Thr Arg Val
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30

<210> 53
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 <212> PRT
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<400> 53
 Ser Ser Tyr Thr Thr Arg Ser Thr Arg Val
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 agcggataac aatttcacac agg

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<223> PCR primer

<400> 55

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<223> Fab'2 antibody fragment

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1 5 10 15

Leu Glu Asp Lys Val Glu Glu Leu Leu Ser Lys Asn Tyr His Leu
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Glu Asn Glu Val Ala Arg Leu Lys Lys Leu Val Gly Glu Arg
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<213> Artificial Sequence

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<400> 57

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<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 58

atgatgatgt gccacgggtcc gtttgatctc cagttcggtc

40

<210> 59

<211> 43

<212> DNA

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<400> 59

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<210> 60

<211> 40

<212> DNA

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<223> PCR primer

<400> 61

gcttctgcgg ccacacaggc ctacgctcag tctgtgctga ctc

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<210> 62

<211> 39

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<223> PCR primer

<400> 62

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<210> 63

<211> 45

<212> DNA

<213> Artificial Sequence

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<223> PCR primer

<400> 63

gtaaattgtat gggcccttgg tggaggaggc actcgagacg gtgac

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<210> 64

<211> 39

<212> DNA

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39

<210> 65

<211> 39

<212> DNA

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<223> PCR primer

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<210> 67
<211> 39
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<223> PCR primer

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<210> 68
<211> 39
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<220>
<223> PCR primer

<400> 68
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<210> 69
<211> 42
<212> DNA
<213> Artificial Sequence

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<400> 69
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<211> 12
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<223> gD tag

<400> 70
Met Ala Asp Pro Asn Arg Phe Arg Gly Lys Asp Leu
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 <213> Artificial Sequence

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 1 5 10 15
 Val Ile Val Gly Leu His Gly Val Arg Gly Lys Tyr Ala Leu Ala
 20 25 30
 Asp Ala Ser Leu Lys Met Ala Asp Pro Asn Arg Phe Arg Gly Lys
 35 40 45
 Asp Leu Pro Val Leu Asp Gln Leu Leu Glu Gly Gly Ala Ala His
 50 55 60
 Tyr Ala Leu Leu Pro Gly
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 1 5 10 15
 Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Tyr Gly Tyr Ser Phe Ala
 20 25 30
 Thr Ser Trp Ile Gly Trp Val Arg Gln Met Pro Gly Arg Gly Leu Glu
 35 40 45
 Trp Met Ala Ile Met Tyr Pro Gly Asn Ser Asp Thr Arg His Asn Pro
 50 55 60
 Ser Phe Glu Asp Gln Val Thr Met Ser Ala Asp Thr Ser Ile Asn Thr
 65 70 75 80
 Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr
 85 90 95
 Tyr Cys Ala Arg Ala Gly Val Ala Gly Gly Ala Phe Asp Leu Trp Gly
 100 105 110
 Lys Gly Thr Met Val Thr Val Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Ala
 130 135 140
 Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr Gly
 145 150 155 160
 Thr Ser Ser Gly Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln
 165 170 175
 His Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Asn Ser Asn Arg
 180 185 190
 Pro Ser Gly Val Pro Asp Arg Phe Ser Ala Ser Lys Ser Gly Asn Thr
 195 200 205

Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
 210 215 220
 Phe Cys Ser Thr Tyr Ala Pro Pro Gly Ile Ile Met Phe Gly Gly Gly
 225 230 235 240
 Thr Lys Leu Thr Val Leu Gly Ala Ala
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 1 5 10 15
 Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
 20 25 30
 Asp Tyr Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Val Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
 65 70 75 80
 Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Ala Arg Trp Ser Gly Glu Asp Ala Phe Asp Ile Trp Gly Gln
 100 105 110
 Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115 120 125
 Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Ser
 130 135 140
 Thr Leu Ser Ala Ser Val Gly Asp Arg Val Ala Ile Thr Cys Arg Ala
 145 150 155 160
 Ser Glu Gly Ile Tyr His Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
 165 170 175
 Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Ala Ser Gly
 180 185 190
 Ala Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp Phe Thr Leu
 195 200 205
 Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln
 210 215 220
 Gln Tyr Ser Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu
 225 230 235 240
 Val Lys Arg Ala Ala
 245

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<400> 74.

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Gly Gly Ser Leu Ser Leu Ser Cys Ala Val Ser Gly Ile Thr Leu Arg
 20      25      30
Thr Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35      40      45
Trp Val Ala Gly Ile Ser Phe Asp Gly Arg Ser Glu Tyr Tyr Ala Asp
 50      55      60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
 65      70      75      80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
 85      90      95
Tyr Cys Ala Arg Asp Arg Gly Ser Tyr Gly Met Asp Val Trp Gly Arg
 100     105     110
Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
 115     120     125
Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser
 130     135     140
Thr Leu Ser Ala Ser Ile Gly Asp Arg Val Thr Ile Thr Cys Arg Ala
 145     150     155     160
Ser Glu Gly Ile Tyr His Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly
 165     170     175
Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser Ser Leu Ala Ser Gly
 180     185     190
Ala Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
 195     200     205
Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln
 210     215     220
Gln Tyr Ser Asn Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu
 225     230     235     240
Ile Leu Arg Ala Ala
 245

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<210> 75

<211> 244

<212> PRT

<213> Artificial Sequence

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<223> single chain antibody (scFv) fragments

<400> 75

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Met Ala Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Arg Pro
 1      5      10      15
Gly Gly Ser Leu Ser Leu Ser Cys Ala Val Ser Gly Ile Thr Leu Arg
 20      25      30
Thr Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
 35      40      45
Trp Val Ala Gly Ile Ser Phe Asp Gly Arg Ser Glu Tyr Tyr Ala Asp
 50      55      60
Ser Val Gln Gly Arg Phe Thr Ile Ser Arg Asp Ser Ser Lys Asn Thr
 65      70      75      80
Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
 85      90      95
Tyr Cys Ala Arg Gly Ala His Tyr Gly Phe Asp Ile Trp Gly Gln Gly
 100     105     110
Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Thr Gly Gly Gly Gly

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| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| Ser | Gly | Gly | Gly | Gly | Ser | Asp | Ile | Gln | Met | Thr | Gln | Ser | Pro | Ser | Thr | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Leu | Ser | Ala | Ser | Ile | Gly | Asp | Arg | Val | Thr | Ile | Thr | Cys | Arg | Ala | Ser | |
| 145 | | | | | 150 | | | | | 155 | | | | | | 160 |
| Glu | Gly | Ile | Tyr | His | Trp | Leu | Ala | Trp | Tyr | Gln | Gln | Lys | Pro | Gly | Lys | |
| | | | | 165 | | | | | 170 | | | | | 175 | | |
| Ala | Pro | Lys | Leu | Leu | Ile | Tyr | Lys | Ala | Ser | Ser | Leu | Ala | Ser | Gly | Ala | |
| | | | 180 | | | | 185 | | | | | | 190 | | | |
| Pro | Ser | Arg | Phe | Ser | Gly | Ser | Gly | Ser | Gly | Thr | Asp | Phe | Thr | Leu | Thr | |
| | | 195 | | | | 200 | | | | | | 205 | | | | |
| Ile | Ser | Ser | Leu | Gln | Pro | Asp | Asp | Phe | Ala | Thr | Tyr | Tyr | Cys | Gln | Gln | |
| | 210 | | | | | 215 | | | | | 220 | | | | | |
| Tyr | Ser | Asn | Tyr | Pro | Leu | Thr | Phe | Gly | Gly | Gly | Thr | Glu | Leu | Glu | Ile | |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 | |
| Lys | Arg | Ala | Ala | | | | | | | | | | | | | |

<210> 76

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<213> Artificial Sequence

<220>

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<221> VARIANT

<222> 208

<223> Xaa = Any Amino Acid

<400> 76

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| Met | Ala | Gln | Val | Gln | Leu | Val | Glu | Ser | Gly | Gly | Gly | Leu | Val | Lys | Pro | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| Gly | Gly | Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Thr | Phe | Ser | |
| | | | 20 | | | | 25 | | | | | | 30 | | | |
| Ser | His | Asn | Met | Asn | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| Trp | Val | Ser | Ser | Ile | Ser | Ser | Ser | Ser | Ser | Tyr | Ile | Tyr | Tyr | Ala | Asp | |
| | 50 | | | | 55 | | | | | | 60 | | | | | |
| Ser | Val | Lys | Gly | Arg | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ala | Lys | Asn | Ser | |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | | |
| Leu | Tyr | Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Tyr | Cys | Ala | Arg | Asp | Arg | Gly | Ser | Thr | Gly | Met | Asp | Val | Trp | Gly | Arg | |
| | | | 100 | | | | 105 | | | | | | 110 | | | |
| Gly | Thr | Leu | Val | Thr | Val | Ser | Ser | Gly | Gly | Gly | Gly | Ser | Gly | Gly | Gly | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| Gly | Ser | Gly | Gly | Gly | Gly | Ser | Asp | Ile | Gln | Met | Thr | Gln | Ser | Pro | Ser | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Thr | Leu | Ser | Ala | Ser | Ile | Gly | Asp | Arg | Val | Thr | Ile | Thr | Cys | Arg | Ala | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Ser | Glu | Gly | Ile | Tyr | His | Trp | Leu | Ala | Trp | Tyr | Gln | Gln | Lys | Pro | Gly | |
| | | | | 165 | | | | | 170 | | | | | 175 | | |
| Lys | Ala | Pro | Lys | Leu | Leu | Ile | Tyr | Lys | Ala | Ser | Ser | Leu | Ala | Ser | Gly | |
| | | | 180 | | | | | 185 | | | | | 190 | | | |
| Ala | Pro | Ser | Arg | Phe | Ser | Gly | Ser | Gly | Ser | Gly | Thr | Asp | Phe | Thr | Xaa | |
| | | 195 | | | | 200 | | | | | | 205 | | | | |
| Thr | Ile | Ser | Ser | Leu | Gln | Pro | Asp | Asp | Phe | Ala | Thr | Tyr | Tyr | Cys | Gln | |

| | | | | |
|-------------------------|---------------------|---------------------|--|-----|
| 210 | | 215 | | 220 |
| Gln Tyr Ser Asn Tyr Pro | Leu Thr Phe Gly Gly | Gly Thr Lys Leu Glu | | |
| 225 | 230 | 235 | | 240 |
| Ile Lys Arg Ala Ala | | | | |
| | 245 | | | |

<210> 77
 <211> 244
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> single chain antibody (scFv) fragments

<400> 77
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 Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Ser
 20 25 30
 Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Ser Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Gly Arg Tyr Phe Asp Val Trp Gly Arg Gly Thr Met Val
 100 105 110
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ser
 130 135 140
 Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val
 145 150 155 160
 Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala
 165 170 175
 Pro Lys Leu Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser
 180 185 190
 Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
 195 200 205
 Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
 210 215 220
 Thr Thr Arg Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val
 225 230 235 240
 Leu Gly Ala Ala